Care of Patients with Emerging Infectious Diseases

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NETEC

Conflict of Interest

- Research Support through institution
  - Astellas

Federal Select Agents – 1st Tier

- Botulinum toxin
- Ebola virus
- Marburg virus
- *Francisella tularensis*
- Variola major
- Variola minor
- *Yersinia pestis*
- *Bacillus anthracis*
- *Burkholderia mallei*
- *Burholderia pseudomallei*
- Several toxins

Other Select Agents

- *Coxiella burnetii*
- Eastern Equine Encephaltis
- Crimean-Congo HF
- Lassa fever virus
- Monkey Pox
- *Rickettsia prowazekii*
- SARS-CoV
- S. American HF
  - Junin
  - Machupo
  - Guanarito
  - Sabia
- Tick-borne encephalitis
- Kyasanur Forest disease
- *Yersinia pestis*

Recently Emerged Viruses

- Chikungunya
- Zika
- MERS-CoV

The Unit at Emory

SCDU Team

- Nineteen Emory Healthcare critical care nurses
- Five Infectious Diseases physicians
- Emory Biosafety Office
- Laboratory personnel
- Materials Management
- Designated Environmental Services personnel
- Occupational Health
- Spiritual Health

Assumptions

- Only direct care providers in the patient room
- No person enters room without mandatory training and demonstrated competency
- Autonomous practice (supported by experts)
  - Ventilator management
  - Continuous renal replacement therapy (CRRT)
  - Physical and occupational therapy
  - Environmental decontamination

Culture of Safety

- Shared accountability for safety
- Effective and assertive communication is central to the safety of the team
- Communication is so important, the team uses rules to govern
  - Direct patient care communication
  - Daily team huddles

Daily Family Huddles

- Held everyday at 0715 when a patient was in the SCDU
- Agenda items included:
  - Clinical update
  - Unit updates
  - Schedule updates
  - Family Rules

Family Rules

- Follow all standard operating procedures to the best of our ability
- Ensure that others follow the standard operating procedures.
- Report all accidents and near misses.
- Report any symptoms which match the pathogen.
- Report any new medical conditions.

Daily Schedules

- It was important to have a schedule in order to maintain a safe, structured environment.
- Staff reported to the unit15-30 minutes prior to scheduled shift, depending on level of PPE required.
- Discussion of daily schedule took place during the family huddle.

Standard Operating Procedures in the Serious Communicable Disease Unit

- Provide consistency in how procedures are performed in the unit
- Allows staff to identify possible deviations when performing the procedure
- Gave staff confidence knowing they were performing procedures consistently

SCDU SOPs

- The care team train and validate competency in the following areas:
  - Donning and doffing of PPE
  - Utilization of the “Buddy System”
  - Waste management protocols
  - Decontamination and containment protocols
  - Specimen handling for diagnostic testing

Standard Operating Procedures

- Donning—patient room and anteroom
- Doffing—patient room and anteroom
- Toileting—ambulatory and non-ambulatory patient
- Waste management
- Spill clean up
- Needle stick/exposure
- Creating chemical mats
- Obtaining and handling lab specimens
- X-ray process
- Transferring equipment between patient rooms
- Cleaning durable medical equipment

The Critical Role of Nursing

- The ability to provide high-level nursing care and supportive care made a significant impact
- 24/7 one-on-one nurses allowed for rapid response to changes and adjustment of care
- Ability to support patients in nutrition, physical therapy, and self care
- Emotional support
- Family support

- Patient- and Family-Centered Model of Care

Patient Evaluation

Physical Examination

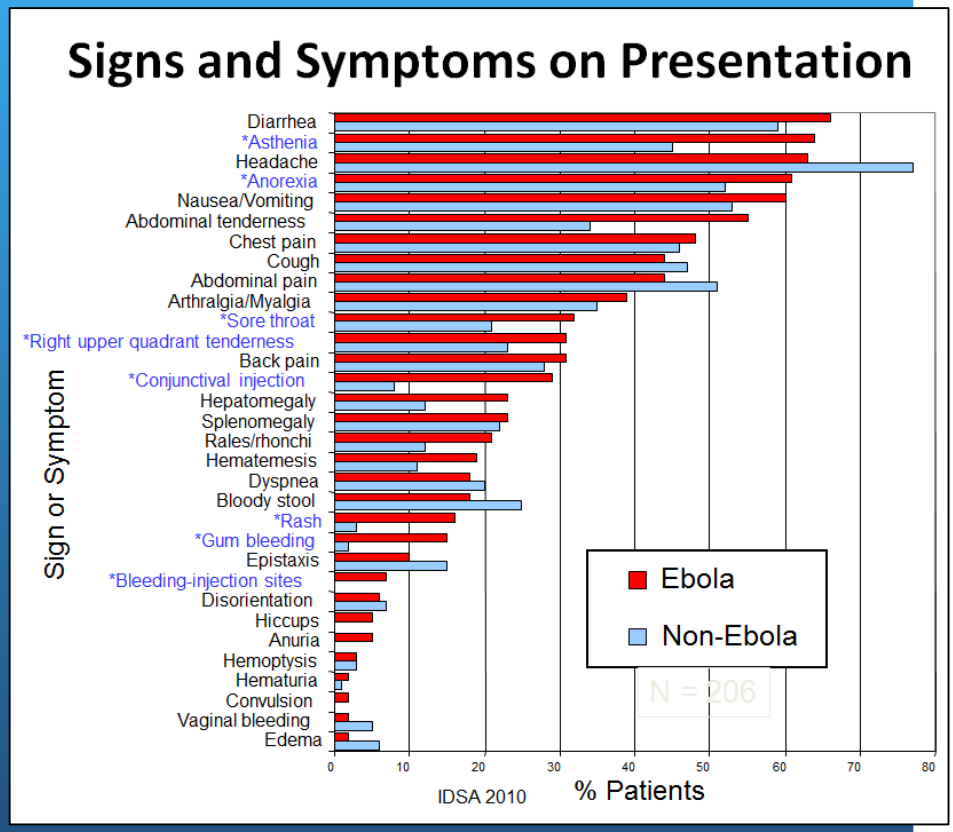
- Palpation
  - Slightly diminished by extra gloves
- Inspection
  - Can be diminished by face shield or goggles
    - Especially if eye protection becomes foggy
    - Plastic can occasionally distort vision
- Auscultation
  - No skin exposed means layer of Tyvek or Tychem between stethoscope and ear drum


SOURCE
MONITOR
indigo
TX
RX
indigo
tab
caps lock
shift
fn

Clinical Signs and Symptoms

Clinical Characteristics of EVD

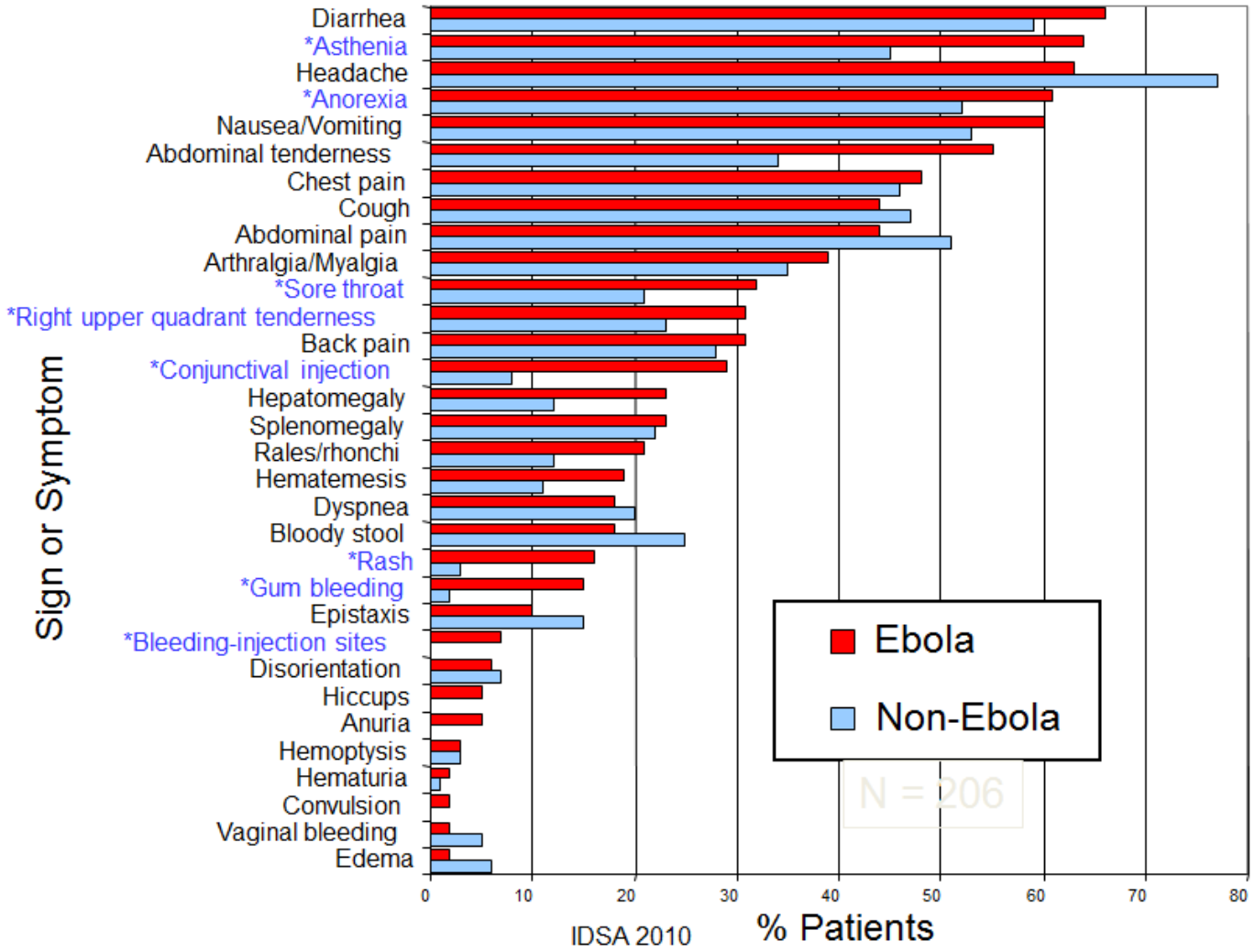
- Acute infection starts as a non-specific febrile illness
  - Fever, severe headache, muscle pain, malaise
- Progression to include GI symptoms
  - diarrhea and vomiting
- May appear 2-21 days after exposure
  - 8-10 days most common



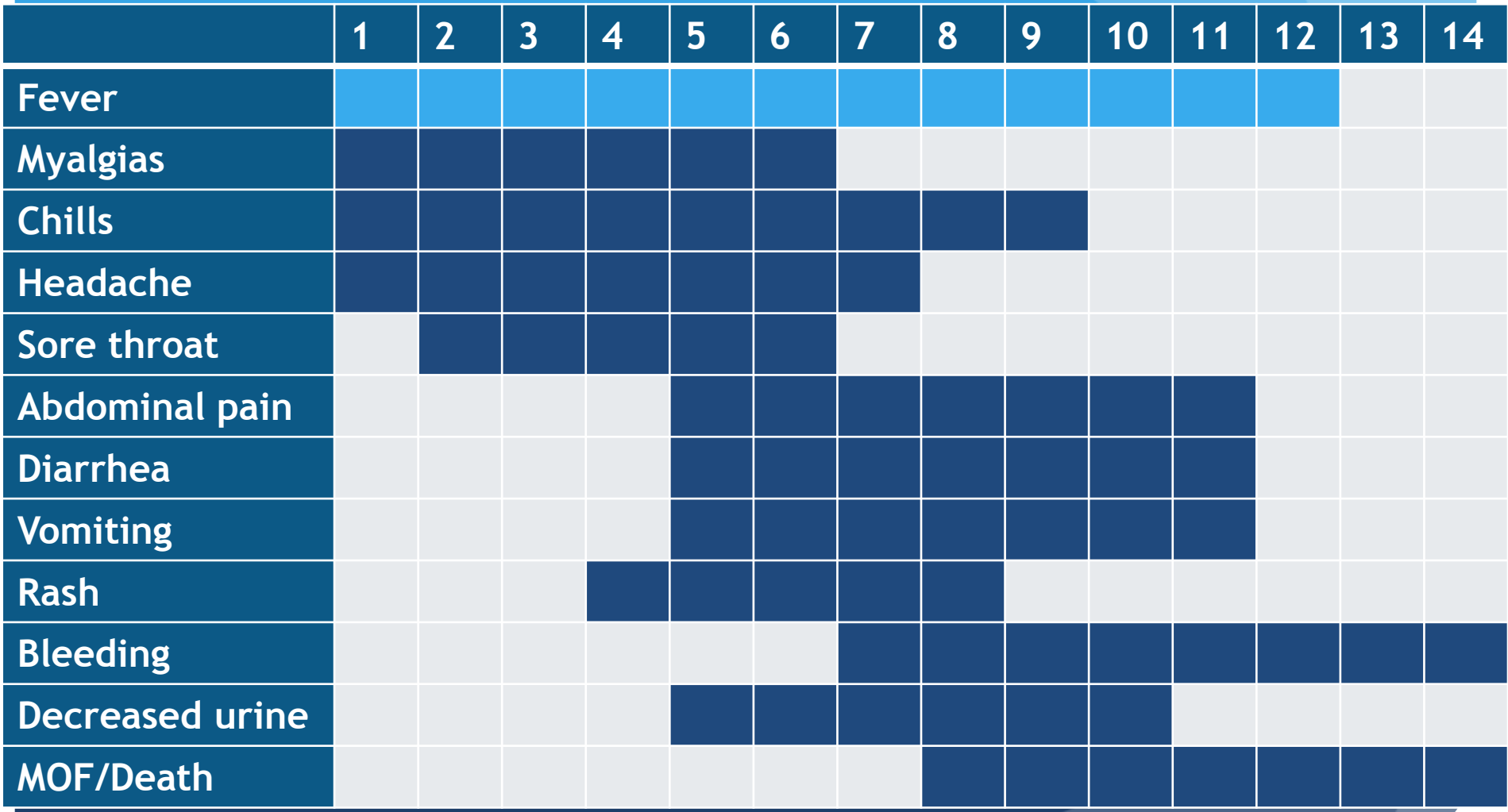
Courtesy of Pierre Rollin, CDC

EMORY HEALTHCARE

Signs and Symptoms on Presentation



Clinical Symptoms and Duration



Clinical Care = Supportive Care

- No proven therapeutics
  - Unclear availability of any experimental agents
  - Limited safety or efficacy data in humans
  - BUT, we received SIGNIFICANT support and advice from CDC, FDA, and medical and scientific colleagues throughout the world

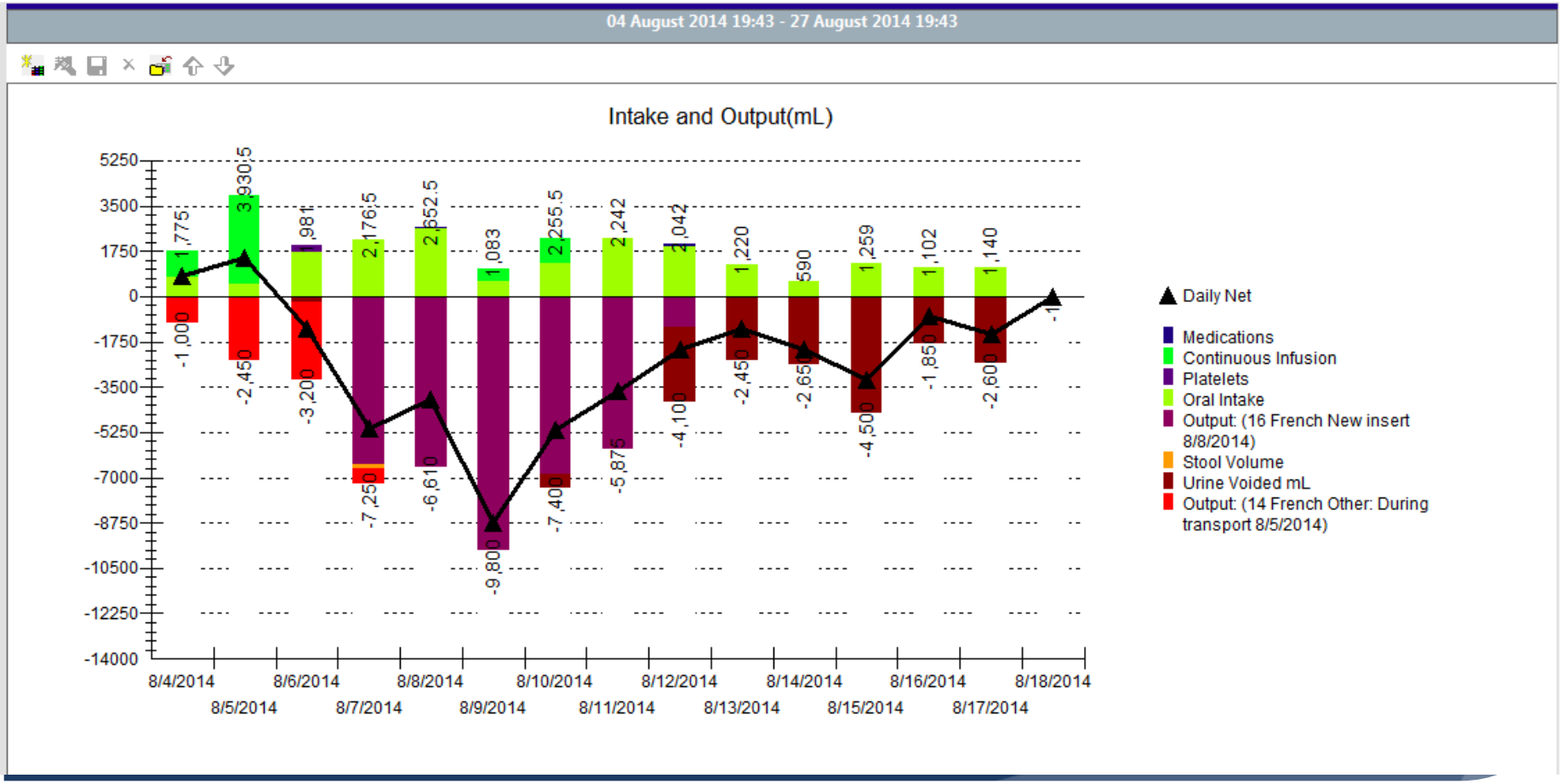
Medical Management

- Supportive Care
  - Fluid management
  - Electrolyte replacement
  - Life support

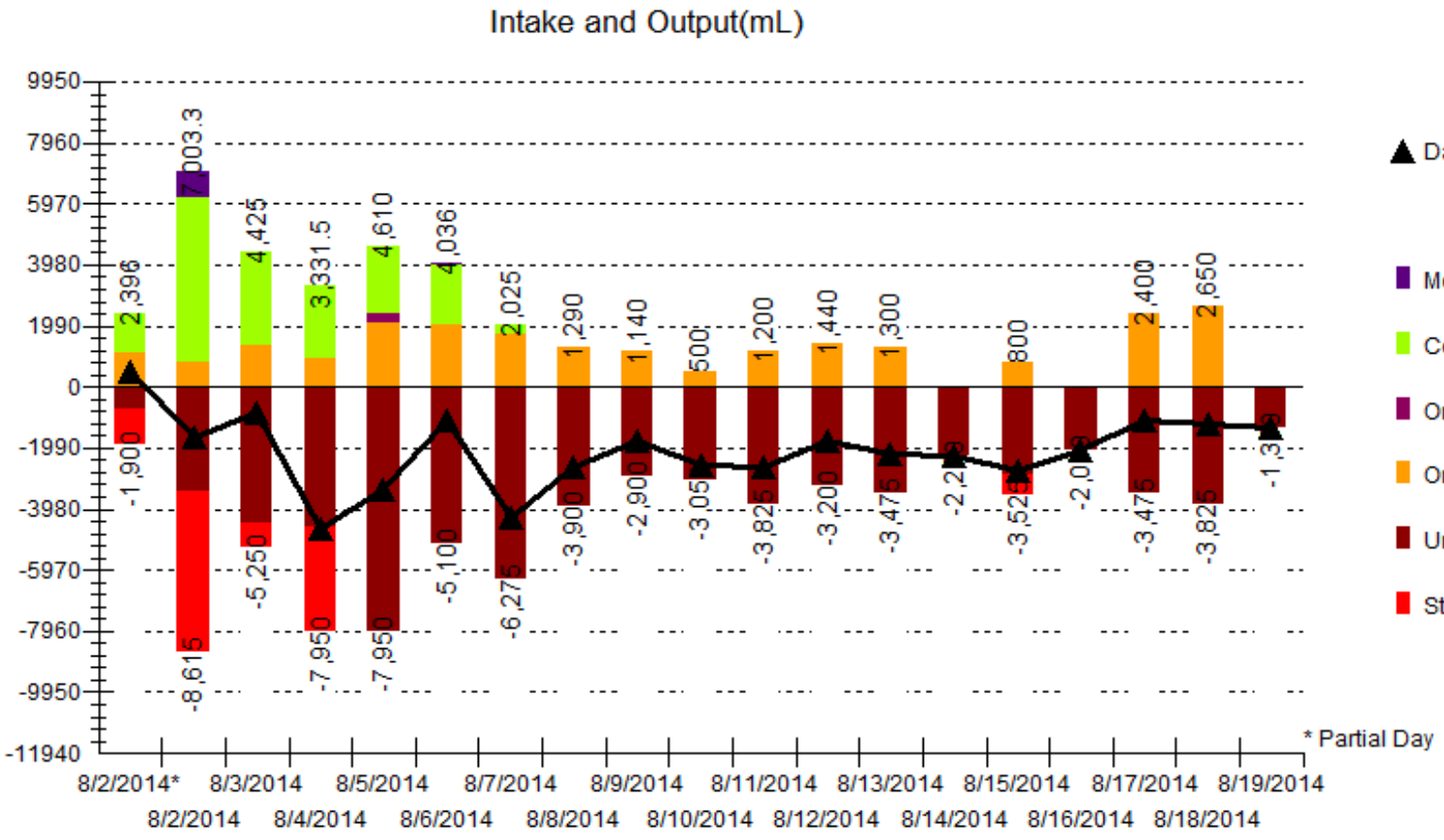
Designated Consulting Physicians

- Critical Care
- Anesthesiology
  - Airway management
- Nephrology
- Pathology
- Others

Fluid Balance



Fluid Balance



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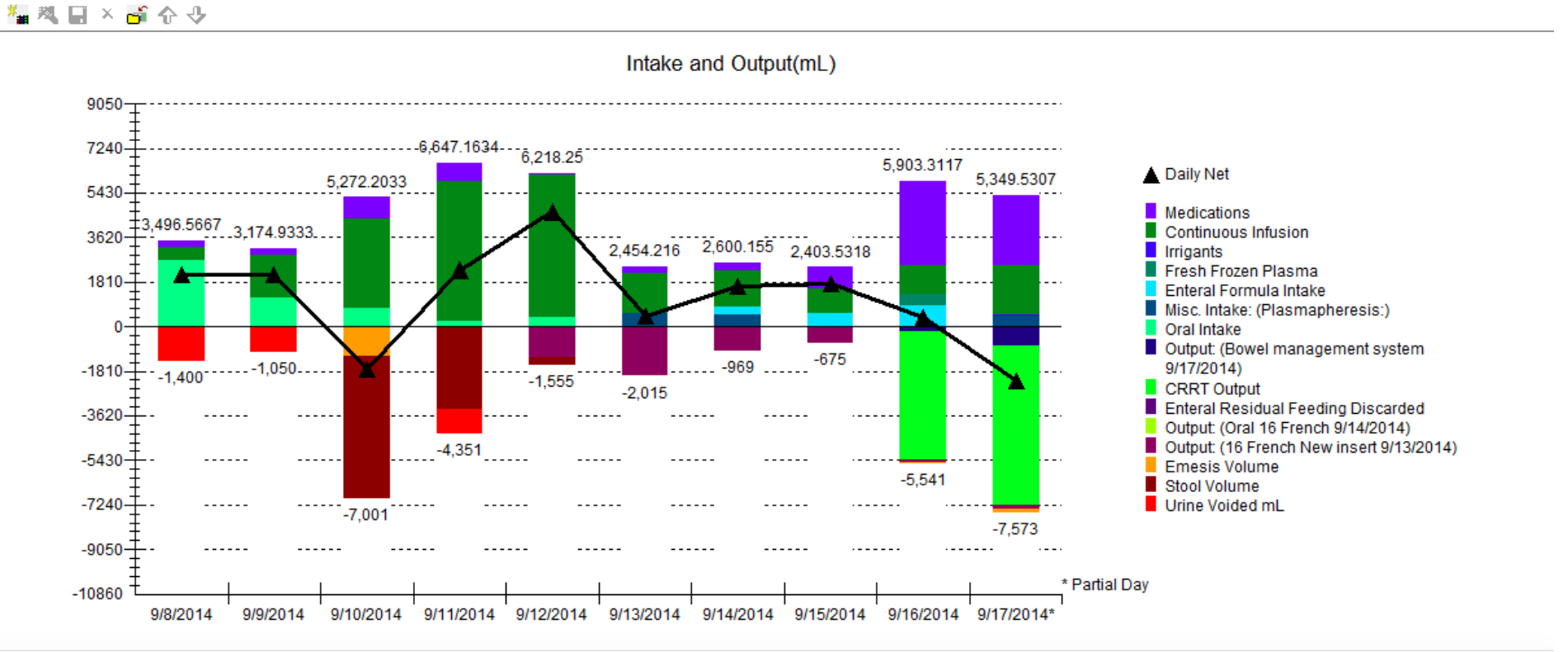

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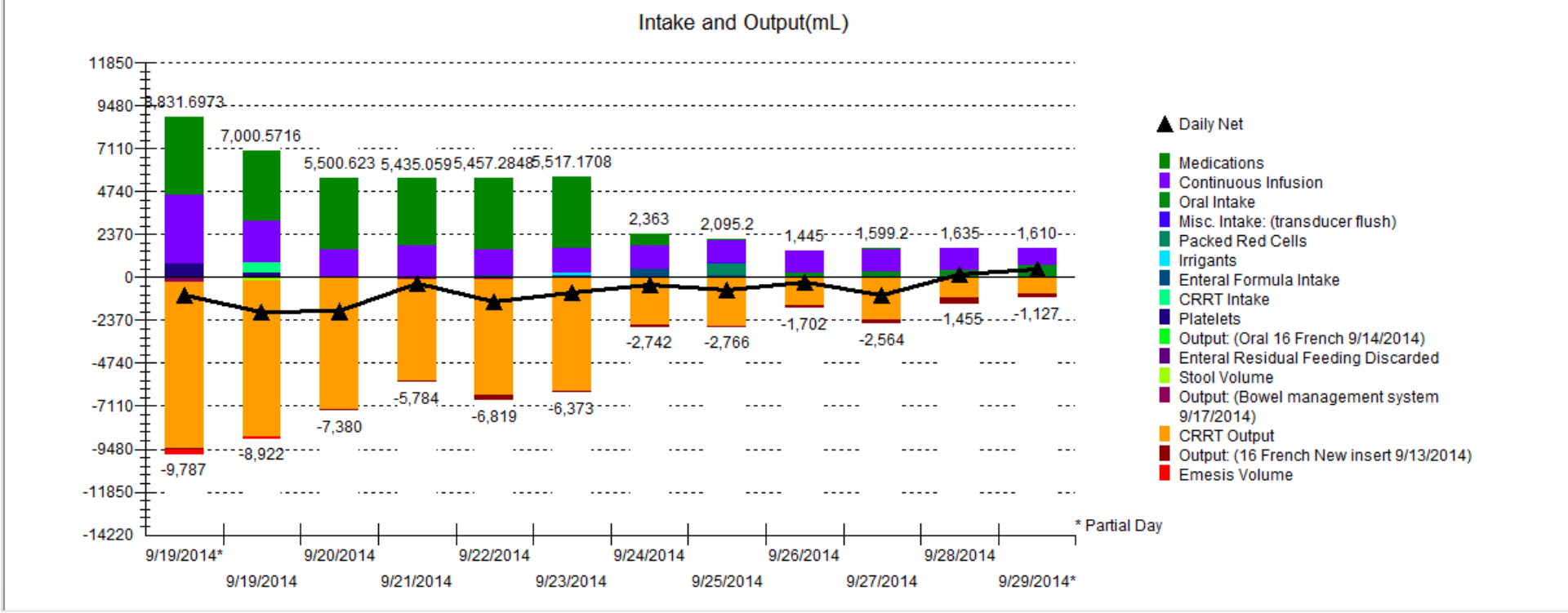

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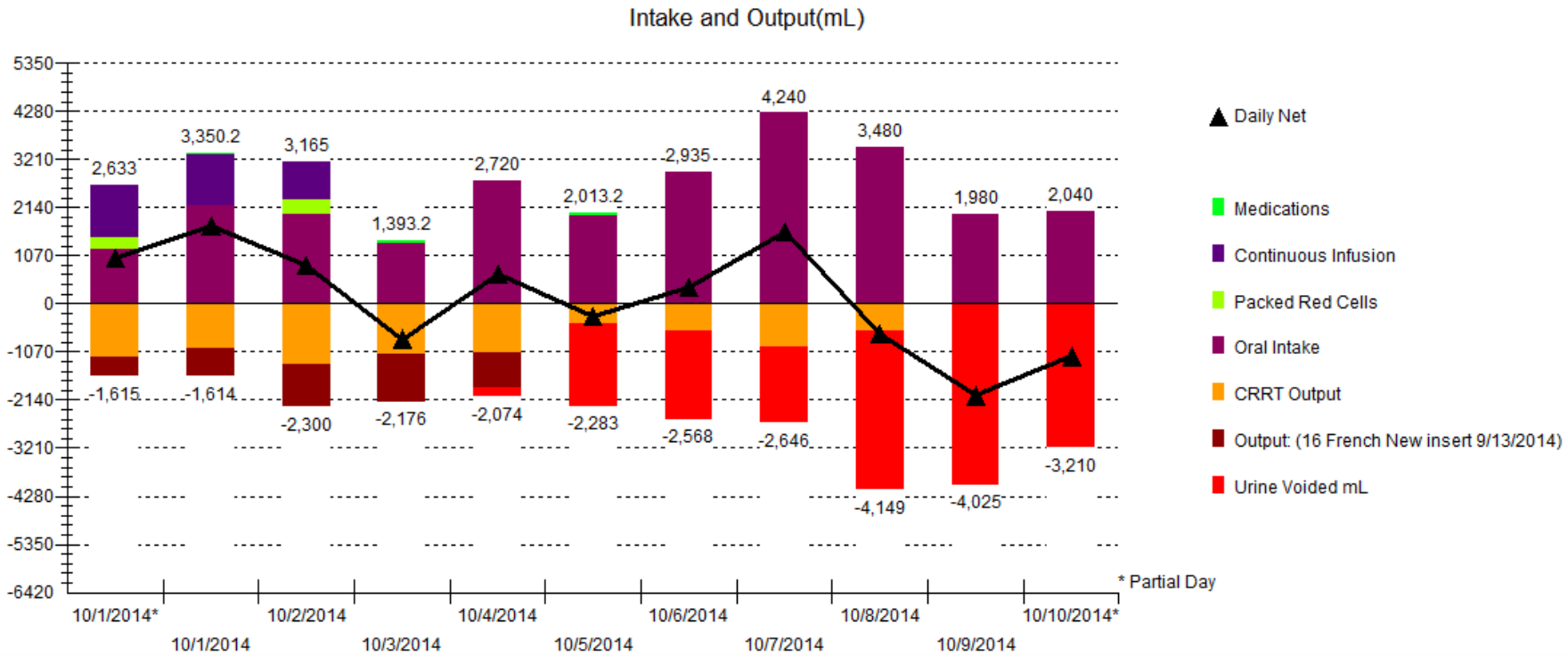
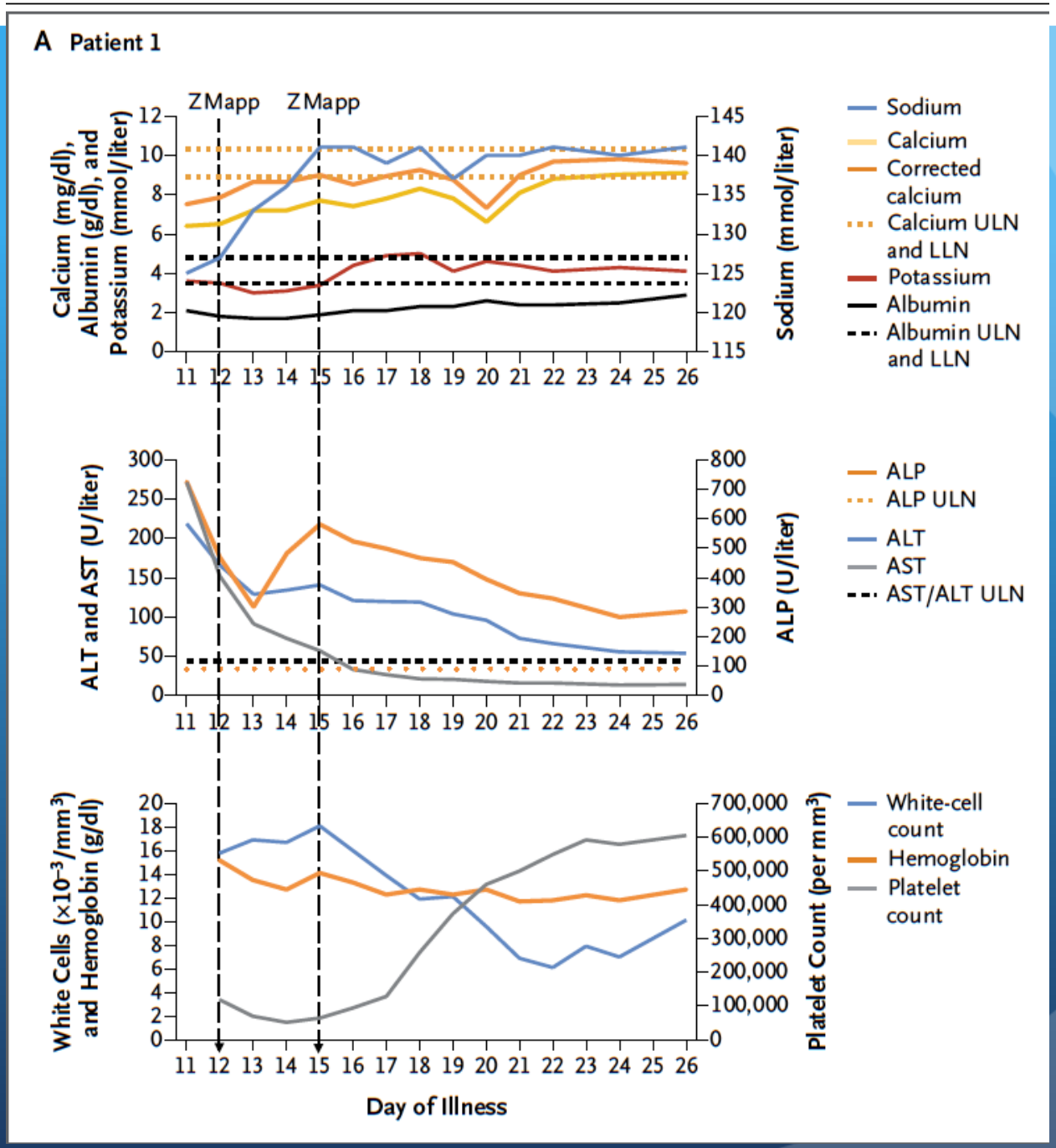
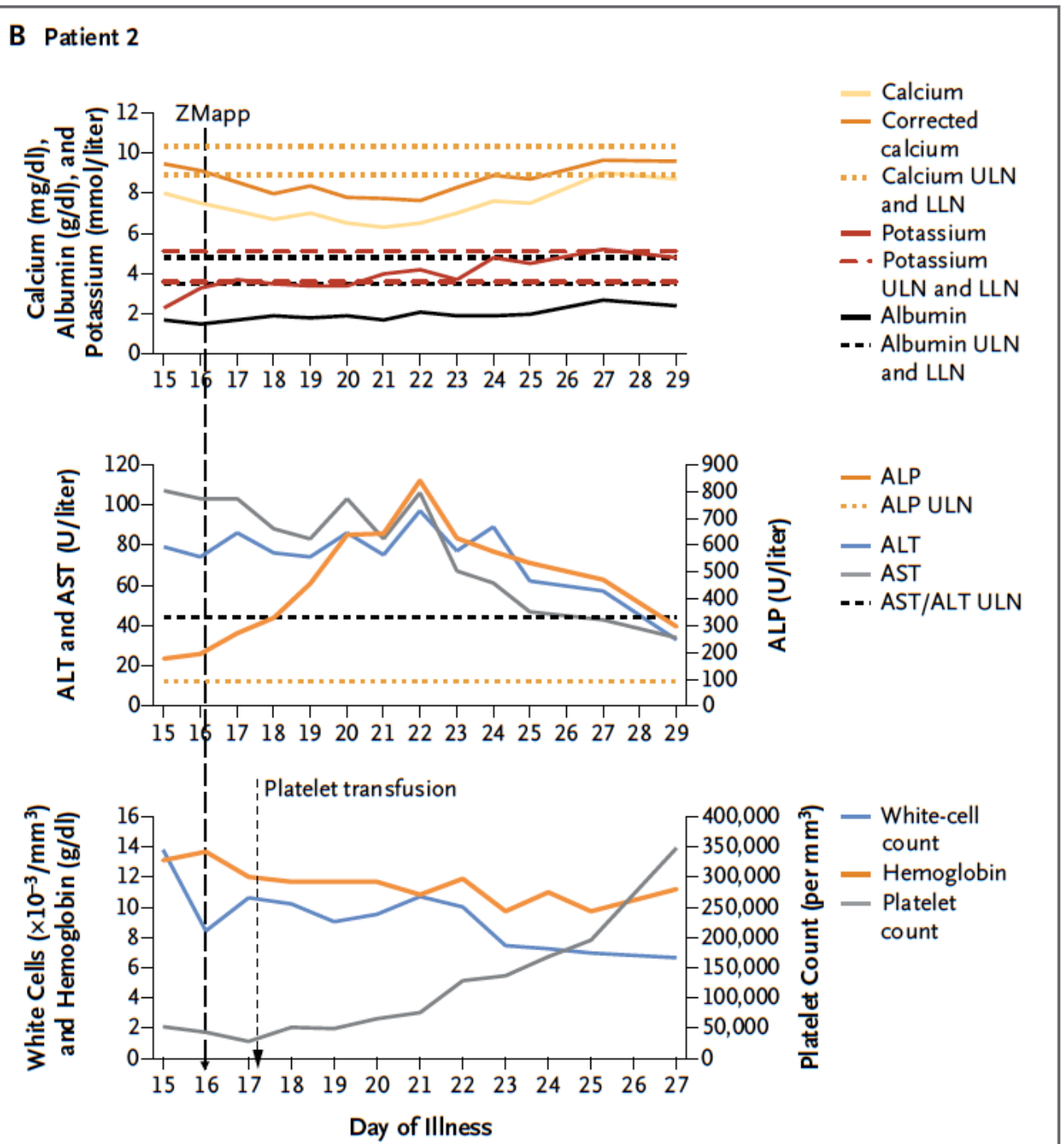



A Patient 1
ZMapp
ZMapp
Calcium (mg/dl), Albumin (g/dl), and Potassium (mmol/liter)
Sodium (mmol/liter)
Sodium
Calcium
Corrected calcium
Calcium ULN and LLN
Potassium
Albumin
Albumin ULN and LLN
ALT and AST (U/liter)
ALP (U/liter)
ALP
ALP ULN
ALT
AST
AST/ALT ULN
White Cells (×10⁻³/mm³) and Hemoglobin (g/dl)
Platelet Count (per mm³)
White-cell count
Hemoglobin
Platelet count
Day of Illness

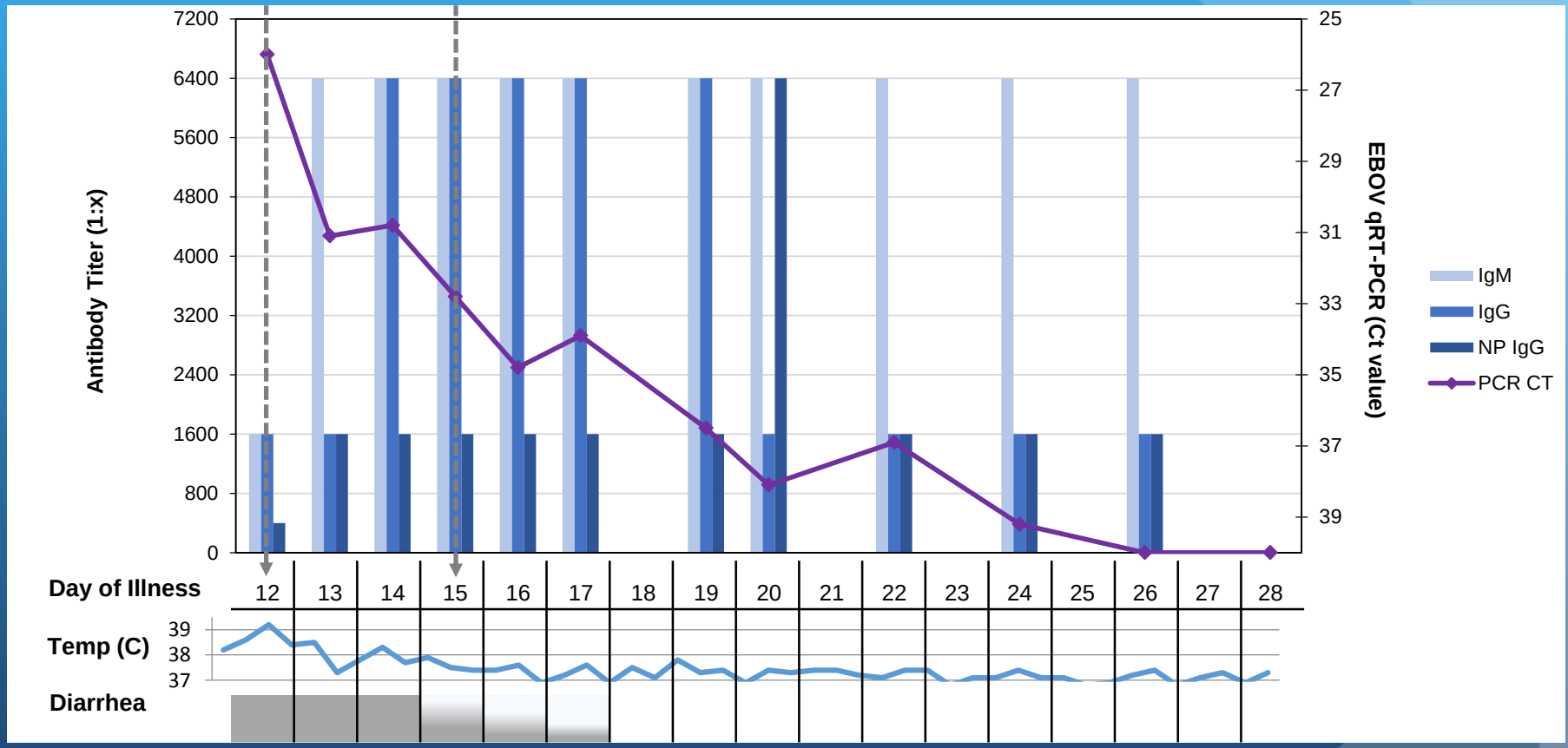

B Patient 2
ZMapp
Calcium (mg/dl), Albumin (g/dl), and Potassium (mmol/liter)
Calcium
Corrected calcium
Calcium ULN and LLN
Potassium
Potassium ULN and LLN
Albumin
Albumin ULN and LLN
ALT and AST (U/liter)
ALP (U/liter)
ALP
ALP ULN
ALT
AST
AST/ALT ULN
Platelet transfusion
White Cells (×10⁻³/mm³) and Hemoglobin (g/dl)
Platelet Count (per mm³)
White-cell count
Hemoglobin
Platelet count
Day of Illness

The Impact of Electrolytes

- Our patients had MARKED electrolyte abnormalities and nutritional deficiencies
  - Hypokalemia, hypocalcemia and hyponatremia
  - Required both intravenous and oral replacement
  - Used oral nutritional supplements including nutritional drinks high in easily absorbed proteins, minerals and vitamins
- Laboratory testing for chemistries was **critical** to provide supportive care

Monitoring Virologic Status

- With the help of the CDC, we monitored ebola in blood
  - Progressive declines in viral loads that correlated with improvements in clinical condition
  - Had very low level of nucleic acid detection for several days despite resolution of symptoms


Antibody Titer (1:x)
7200
6400
5600
4800
4000
3200
2400
1600
800
0
EBOV qRT-PCR (Ct value)
25
27
29
31
33
35
37
39
IgM
IgG
NP IgG
PCR CT
Day of Illness
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
Temp (C)
39
38
37
Diarrhea

Experimental Therapies

Therapy	Mechanism	Status
Convalescent plasma	Provide anti-EBOV antibodies	• Studies have not shown a clear benefit • Has been used in multiple evacuated patients in this outbreak
Hyperimmune globulin from immunized animals or previously infected humans	Concentrated plasma to provide high titers of neutralizing antibody	• Not currently available. • Work in horses and cattle are underway
ZMapp (Mapp Biopharmaceutical Inc.)	Cocktail of three chimeric mouse human monoclonal antibodies targeting the GP envelope protein	• Very promising data in macaques • No human trials • Very limited supply
TKM-100802 Lipid (TKM-Ebola; Tekmira)	Nanoparticle Small interfering Ribonucleic acid (siRNA) Targets two essential viral genes to stop the virus from replicating	• single-dose phase 1 study in healthy volunteers found side effects including headache, dizziness, chest tightness and raised heart rate at high doses. • A limited number of treatment courses

Experimental Therapies

Therapy	Mechanism	Status
AVI 7537 (Sarepta)	Phosphorodiamidate oligonucleotide	• Monkey studies showed 60-80% when given at the time of infection • Tolerability has been demonstrated in early studies. • No human grade availability until late October
Favipiravir/T-705 (Toyama Chemical/ Fuji Film)	Selective inhibition of viral RNA-dependent RNA polymerase Does not inhibit RNA or DNA synthesis in mammalian cells	• Effective against EVD in mice, but in animal monkey study only 1/6 survived • Approved in Japan for influenza treatment under special circumstances. • ~10 000 treatment courses may available
BCX4430 (Biocryst)		• 83-100% survival in rodents with EVD • Effective in animals 48 hours after infection with the lethal Marburg virus • Testing for EVD in monkeys is underway
Brincidofovir (CMX001) (Chimerix)	lipid conjugate of the nucleotide analog, cidofovir (CDV) uses endogenous lipid uptake pathways to achieve high intracellular concentrations	• In vitro data at CDC showing good anti-EBOV activity • Has been used in 4 patients

Experimental Therapies

Therapy	Mechanism	Status
Chimpanzee adenovirus serotype 3 (ChAd3) vaccine	Uses a chimpanzee adenovirus that does not grow Contains the gene for EVD surface protein	• 16/16 monkeys were protected from a lethal dose by a single dose of the vaccine • Trials in humans ongoing • Approximately 15 000 doses might be available by the end of 2014
Recombinant Vesicular Stomatitis Virus (rVSV) vaccine	Recombinant VSV vector expressing ebola GP protein to induce EBOV-specific immune responses	• 20/ 20 monkeys protected from a lethal dose of EVD • Animals with weakened immunity were not harmed by rVSV-EVD • Unknown if rVSV-EVD will grow in humans, which would affect immunogenicity and safety • Phase 1 trials underway • ~800 doses available

Conclusions from our experience

- Patients with Ebola can be safely cared for in our healthcare system
- We do expect a lower mortality rate than in under-developed healthcare systems
- Much can be learned about patient management that can be fed back to facilities with lesser levels of infrastructure
- Communication is critical
- Comprehensive, multidisciplinary patient- and family-centered models of care can be delivered even in extreme circumstances

Other agents

Chemoprophylaxis and Vaccination Post Exposure

- Friedlander et al. JID 1993;176:1239-43
- Following exposure to a lethal inhaled dose of *B. anthracis*, 10 rhesus monkeys in each of 6 groups

Group Antibiotics given for 30 days	Survival after 1st challenge	Survival after rechallenge
Penicillin	7/10	0/7
Ciprofloxacin	8/9	0/8
Doxycycline	9/10	0/9
Doxycycline+vaccine(2)	9/9	8/9
Vaccine(2)	2/10	
Saline	1/10	

Treatment Options

- Penicillin
  - resistance occurs naturally
- Doxycycline
  - resistance has been engineered
- Ciprofloxacin
  - Other fluoroquinolones likely active
  - May be combined with rifampin, vancomycin, imipenem, chloramphenicol, penicillin and ampicillin, clindamycin, or clarithromycin in severe disease
- Experimental treatment: anthrax IG

Botulism: Treatment/Prophylaxis

- Ventilatory assistance and supportive care
- Botulinum antitoxin
  - Trivalent equine product against types A,B, and E available from CDC
  - Most effective if given early
- Antibiotics for wound botulism
  - Penicillin
- Vaccine investigational
- Infection Control – human-to-human transmission does not occur

Plague: Medical Management

- Antibiotic therapy
  - Gentamicin or Streptomycin
  - Tetracyclines
  - Sulfonamides
  - Chloramphenicol (meningitis/pleuritis)

Unknown or Emerging Pathogens

- Most likely to be viral
  - Probably won't have an effective vaccine for years,
    - If ever (HIV)
  - May have effective antivirals
    - Pre-existing antivirals but testing will need to be done
    - Lamivudine for EVD
- Probably won't create zombies

Thank you

Questions?